



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|--|-------------|----------------------|------------------------------------|------------------------|
| 10/510,454 | 10/04/2004 | Hector Knight Castro | 1483 WO/US | 2287 |
| 7590 Tim A Cheatham Mallinckrodt Inc 675 McDonnell Boulevard PO Box 5840 St Louis, MO 63134 | | | EXAMINER PERREIRA, MELISSA JEAN | |
| | | | ART UNIT 1618 | PAPER NUMBER |
| | | | MAIL DATE 02/25/2009 | DELIVERY MODE PAPER |

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/510,454

Applicant(s)

KNIGHT CASTRO ET AL.

Examiner

MELISSA PERREIRA

Art Unit

1618

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 January 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2 and 4-18 is/are pending in the application.
- 4a) Of the above claim(s) 6-15 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,2,4-6 and 16-18 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SI/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1/5/09 has been entered.

Claims and Previous Rejections Status

2. Claims 1,2 and 4-18 are pending in the application. Claims 6-15 are withdrawn from consideration. Claims 17 and 18 are newly added in the amendment filed 1/5/09.
3. The rejection Claims 1,2,4,5 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Supplement to the Manual and Operating Instructions, FDG Synthesizers, Nuclear Interface GmbH, 11/21/01) in view of Dumhaut et al. (US 6,172,207B1) and further in view of Asai et al. (US 5,536,491) and Stone-Elander et al. (5,308,944A) is maintained and modified.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. Claims 1,2,4,5 and 16-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over the Manual and Operating Instructions, Nuclear Interface GmbH, including the Supplement FDG Synthesizers, 11/21/01) in view of Dumhaut et al. (US 6,172,207B1) and further in view of Asai et al. (US 5,536,491) and evidenced by Stone-Elander et al. (5,308,944A).
6. The Manual and Operating Instructions discloses the method of improving the stability (avoiding decomposition) of a FDG solution. The method involves adjusting the pH of the FDG solution to 5.5 with a buffered product. It is important that the pH of the solution does not reach pH=6 because at this pH considerable degradation starts (p38). The Manual and Operating Instructions discloses heating the FDG with a buffer to a temperature of 135 degrees (4.3, p10, two sterilizing cycles) which encompasses the autoclave temperature of the instant invention as evidenced in the specification which teaches of an autoclave temperature of 134 degrees (spec, p4, line 1).
7. The Manual and Operating Instructions does not disclose that the FDG is labeled with 18F, that the buffering agent is citrate or that the solution is autoclaved.
8. Dumhaut et al. (US 6,172,207B1) discloses an 18F-FDG solution for NMR (example; column 3, line 28; column 6, line 33) where the pH adjustment and isotonicity to injectable standards of the final solution is performed by adding a buffer. The buffer may be a solution of citrate or sodium phosphate, tris or any other injectable buffer (column 5, lines 44-54). The disclosure states that the collected labeled compound is purified, filtered or sterilized (claim 22).

9. Asai et al. (US 5,536,491) discloses the sterilization of ^{19}F -labeled MRI contrast agents via autoclave (example 30).

10. At the time of the invention it would have been obvious to one ordinarily skilled in the art to substitute the citrate buffer of Dumhaut et al. for another known analogous buffer disclosed in the Manual and Operating Instructions for the method of improving the stability of a FDG solution. It is obvious to those skilled in the art to make known substitutions on compounds that are similar in structure and function to observe the effects on the function of such compounds and to use the observations/data to further manipulate a compound to generate the desired effect.

11. At the time of the invention it would have been obvious to one skilled in the art to use the known sterilization method of autoclaving a fluorine substituted contrast agent solution which is taught by Asai et al. for the sterilization method of Dumhaut et al. (see claim 22) with predictable results, such as providing a sterilized solution for the NMR/MRI imaging. The ^{18}F isotope is stable against high temperature (as evidenced by Stone-Elander et al., see fig. 7; column 2, lines 22-25) and therefore will be capable of being successfully autoclaved/sterilized and maintain radiochemical purity after being autoclaved. FDG is also stable at a temperature of 135 degrees (where the specification teaches of an autoclave temperature of 134 degrees (spec, p4, line 1)) as evidenced by the Manual and Operating Instructions and therefore it would have been obvious to one ordinarily skilled in the art to autoclave ^{18}F -FDG in a citrate buffer as taught by Dumhaut et al. up to and including 135 degrees.

Response to Arguments

12. Applicant's arguments filed 1/5/09 have been fully considered but they are not persuasive.

13. Applicant asserts that the Manual and Operating Instructions reference does not qualify as prior art as it is not proven that the printed publication has been disseminated or otherwise made available or that the mere listing of a reference in an IDS is not viewed as an admission that the reference is prior art.

14. The Manual and Operating Instructions reference is indeed a manual for operating instructions of a laboratory instrument and thus it is obvious that the manual would be distributed to those who purchase/obtain such an instrument. Also, the Manual and Operating Instructions states that "for more information about programming the time list please refer to the separate software manual". Therefore it is obvious that a person who purchases/obtains such as manual would also receive a separate software manual to provide for instructions.

15. A REFERENCE IS A "PRINTED PUBLICATION" IF IT IS ACCESSIBLE TO THE PUBLIC and EXAMINER NEED NOT PROVE ANYONE ACTUALLY LOOKED AT THE DOCUMENT

16. A reference is proven to be a "printed publication" "upon a satisfactory showing that such document has been disseminated or otherwise made available to the extent that persons interested and ordinarily skilled in the subject matter or art, exercising reasonable diligence, can locate it." In re Wyer, 655 F.2d 221, 210 USPQ 790 (CCPA

1981) (quoting I.C.E. Corp. v. Armco Steel Corp., 250 F. Supp. 738, 743, 148 USPQ 537, 540 (SDNY 1966)) ("We agree that printed publication' should be approached as a unitary concept. The traditional dichotomy between printed' and publication' is no longer valid. Given the state of technology in document duplication, data storage, and data retrieval systems, the probability of dissemination' of an item very often has little to do with whether or not it is printed' in the sense of that word when it was introduced into the patent statutes in 1836. In any event, interpretation of the words printed' and publication' to mean probability of dissemination' and public accessibility' respectively, now seems to render their use in the phrase printed publication' somewhat redundant.")
In re Wyer, 655 F.2d at 226, 210 USPQ at 794. See MPEP § 2128 [R-5]

17. Applicant asserts that Dumhaut et al. is not concerned with the preparation of a 18-F-FDG solution that possess stability sufficient to withstand sterilization by autoclaving and does not even reference autoclaving.

18. The method of Dumhaut et al. was not used to teach of autoclaving but used to teach of the sterilization and of buffering an 18F-FDG solution for NMR with a citrate buffer. The Manual and Operating Instructions reference teaches of heating a buffered FDG solution to a temperature of 135 degrees and therefore it would have been obvious to substitute the citrate buffer of Dumhaut et al. for an analogous buffer, such as that of the Manual and Operating Instructions. It is obvious to those skilled in the art to make known substitutions on compounds that are similar in structure and function to observe the effects on the function of such compounds and to use the observations/data to further manipulate a compound to generate the desired effect.

19. The combined references of Asai et al. and Stone-Elander et al. were used to teach of the sterilization of 18F-labeled MRI contrast agents via autoclave where Asai et al. teaches of autoclaving 19F-labeled compounds and Stone-Elander et al. teaches that 18F is stable at elevated temperatures. Thus, it would have been obvious that 18F-labeled NMR/MRI agents may be autoclaved. In addition, it would have been obvious to one of ordinary skill that a buffered FDG solution may be autoclaved since FDG is stable at a temperature of 135 degrees as the specification teaches that autoclaving is at a temperature of 134 degrees. Therefore it would have been obvious to one of ordinary skill that an 18F-FDG may be successfully autoclaved.

20. Applicant asserts that Asai et al. teaches of a 19F-labeled MRI contrast agents via autoclaving but points out that a 19F-labeled MRI contrast agent is distinctly different from an 18-F labeled radionuclide. Applicant asserts that the failure or success of autoclaving a non-radioactive 19F cyclic polyamine molecule used in MRI procedures would not suggest to one skilled in the art that a radioactive 18F-FDG solution comprising a weak acid could be autoclaved wherein radiochemical purity is maintained.

21. The reference of Asai et al. was used to teach of the autoclaving of fluorine containing MRI contrast agent while Stone-Elander et al. was used to teach that the 18F isotope will be stable when subjected to elevated temperatures, such as 134 degrees where the specification teaches autoclaving at 134 degrees (specification, p4, line 1). FDG can also be heated to 135 degrees (The Manual and Operating Instructions), thus it would have been obvious to one of ordinary skill that the citrate buffer 18F-FDG solution of Dumhaut et al. can be autoclaved at 135 degrees.

22. Applicant asserts that it appears that Stone-Elander et al. is cited for disclosing that the ^{18}F isotope of the compounds disclosed therein will be stable when subjected to elevated temperatures. Applicant asserts that the compounds of Stone-Elander et al. are structurally very different from the ^{18}F -FDG of the present invention.

23. The reference of Stone-Elander et al. was used to teach that ^{18}F can tolerate a temperature of 135 degrees and where the specification teaches autoclaving at 134 degrees (specification, p4, line 1). FDG can be heated to 135 degrees (The Manual and Operating Instructions) and it is disclosed that ^{18}F can tolerate a temperature of 135 degrees (Stone-Elander et al.), thus it would have been obvious to one of ordinary skill that the buffered ^{18}F -FDG citrate solution of Dumhaut et al. can be autoclaved at 135 degrees.

New Ground of Rejection Necessitated by the Amendment

Claim Rejections - 35 USC § 112

24. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

25. Claims 1,2,4,5 and 16-18 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the instant claims do not include an active step of autoclaving.

Conclusion

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MELISSA PERREIRA whose telephone number is (571)272-1354. The examiner can normally be reached on 9am-5pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

/Melissa Perreira/
Examiner, Art Unit 1618